NavMed 369

UNITED STATES NAVY

# MEDICAL NEWS LETTER

Editor - Captain F. W. Farrar, MC, USN

Vol. 12 Friday, 19 November 1948 No. 11

NavMed 369

UNITED STATES NAVY

# MEDICAL NEWS LETTER

Editor - Captain F. W. Farrar, MC, USN

Vol. 12 Friday, 19 November 1948 No. 11

TABLE OF CONTENTS



* * * * * *

* * * * *

Procaine Penicillin Preparations: For some time it has been known that a mixture of concentrated solutions of penicillin and procaine resulted in the formation of crystals which were identified as the procaine salt of penicillin. Whereas the previously available salts (sodium, potassium, and calcium) are highly soluble in aqueous solutions and body fluids, the procaine salt is relatively insoluble. This property forms the basis of a new principle of penicillin administration. As a result of the low solubility of procaine penicillin, a repository injection of a suspension of this salt in oil or water results in delayed absorption and prolonged blood concentrations. This report presents the results of studies on absorption following the intramuscular injection of procaine penicillin.

Crystalline procaine penicillin is usually prepared by the double decomposition of sodium penicillin G and procaine hydrochloride. The original commercial preparations were suspended in refined sesame or peanut oil so that 300,000 units were present in 1 c.c. as a free-flowing fluid material. Such a preparation need not be refrigerated because it will remain stable for at least one year at room temperature. Because the procaine penicillin on standing separates from the oil and because of the necessity for vigorous agitation in order to re-establish the suspension, detergents such as "Tween 80" (Sorbitan mono-oleate, polypoxyalkylene derivative) and "Span 80" (Sorbitan mono-oleate) have been added to facilitate resuspension. These measures have been only partially successful. Other investigators have added aluminum nonostearate to the mixture to maintain the suspension. The addition of aluminum monostearate to procaine penicillin in oil results in a gel formation which maintains the suspension of the penicillin in the oil.

Peanut or sesame oil was originally employed as a vehicle for injecting procaine penicillin because it was impossible to prepare injectable water suspensions of this penicillin salt. Recently it has been demonstrated that the addition of dried sodium carboxymethylcellulose to dry crystalline procaine penicillin results in a stable suspension in diluents containing water. Sodium carboxymethylcellulose in aqueous solution forms a viscous gel which maintains the procaine penicillin in suspension as discrete particles. This has eliminated the necessity for the use of oils, which have been shown to be antigenic and which may cause serious complications if they are injected accidentally into a blood vessel.

All of the procaine penicillin preparations can be withdrawn from the vial and administered through a 19- or 20-gauge needle. For the preparations containing aluminum monostearate or sodium carboxymethylcellulose, dry syringes and needles are not needed, nor are they needed for procaine penicillin in oil if the injection is made immediately after the syringe is filled.

The concentrations of penicillin in the blood at various intervals were determined (according to the method of Randall and associates) following the intramuscular injection of (1) 300,000 units of procaine penicillin in oil, (2) 300,000

units of procaine penicillin in oil plus 2-percent W/V aluminum monostearate, and (3) 300,000 units of procaine penicillin plus sodium carboxymethylcellulose in aqueous suspension. The results are shown in the table below.

| PREPARATION | | HOUR | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 12 | 16 | 20 | 24 | 36 | 48 | 60 | 72 | 96 | 120 | 144 |
| Procaine penicillin in oil | Median levels (U./c.c.) | 0.375 | 0.375 | 0.25 | 0.125 | 0.031 | 0.031 | | | | | |
| | Percentage of patients with assayable levels* | 100 | 100 | 100 | 96 | 57 | 36 | | | | | |
| Procaine penicillin (particles less than 5 $\mu$) in oil plus aluminum monostearate | Median levels (U./c.c.) | | | | 0.25 | | 0.125 | | 0.062 | 0.062 | 0.031 | 0 |
| | Percentage of patients with assayable levels* | | | | 100 | | 100 | | 100 | 100 | 100 | 42 |
| Procaine penicillin plus sodium carboxymethylcellulose | Median levels (U./c.c.) | 0.5 | 0.25 | 0.25 | 0.125 | 0.125 | .062 | 0.062 | 0 | | | |
| | Percentage of patients with assayable levels* | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 25 | | | |

At least twenty-five patients were studied at each time interval indicated for the various preparations.
*Method of Randall and associates[7] detecting 0.03 unit per cubic centimeter and higher.

From the table it is apparent that the addition of aluminum monostearate not only stabilizes the suspension of procaine penicillin in oil but also results in prolongation of the concentrations of penicillin in the blood. Preparations containing particles of penicillin less than 5 $\mu$ in size resulted in measurable blood concentrations in all patients at 24, 48, 72, 96, and 120 hours after injection. When large-particle procaine penicillin crystals are employed in this mixture, the concentrations of penicillin in the blood are not so prolonged. (See News Letter of 5 November 1948, last paragraph, page 23.)

While this study was in progress, several of the commercially available lots of procaine penicillin in oil were found to be inferior in that only about from one half to one third of the patients had detectable levels in the blood at the twenty-fourth hour following the injection of 300,000 units of procaine penicillin in oil (1 c.c.). It was found that in conversion to mass production, crystallization was not carefully controlled, so that large particles of procaine penicillin were produced. In grinding these particles to sizes capable of passage through 19 or 20-gauge needles, relatively large amounts of procaine penicillin dust or flour were produced. The fine particles comprising this dust or flour are dissolved and absorbed relatively rapidly, so that prolonged blood concentrations are not maintained. (The manufacturers have taken steps to eliminate the fine particles from their preparations.) Therefore, the blood concentrations obtained after the injection of preparations of this kind have not been included in the table above.

Blood concentrations were determined in 17 patients who were receiving 300,000 units of the procaine penicillin in oil preparations every 12 hours and in 14 subjects who received 600,000 units (2 c.c.) every twelve hours. Upon such regimens the blood concentrations at the twelfth hour were at least 0.125 unit per cubic centimeter and usually 0.25 and 0.5 unit per cubic centimeter. There were no significant differences between the two doses.

The authors have withdrawn from containers and administered without difficulty procaine penicillin preparations with syringes sterilized by boiling but damp when used. Procaine penicillin preparations maintain blood concentrations

of penicillin which are adequate for most purposes. The best preparations of penicillin in oil and wax give detectable levels in 92 percent of the patients with 300,000 units at the twenty-fourth hour, but the average preparation produces such levels in only about 85 percent of patients. Similar doses of procaine penicillin in oil consistently result in adequate concentrations in at least 94 percent of the patients and in 100 percent of patients when optimal preparations are used. Not only do a greater percentage of patients have detectable concentrations at the twenty-fourth hour, but the concentrations are usually from two- to fourfold higher than those obtained with penicillin in oil and wax. This is undoubtedly explained by the fact that the release of penicillin from the procaine combination is slow, resulting in a flat and sustained curve, but the one produced by the oil and wax preparation is peaked in the early hours and is not as well sustained. The problem of separation of the procaine penicillin from the oil has been overcome by the addition of aluminum monostearate. With the use of carboxymethylcellulose the procaine penicillin can be administered in aqueous suspension.

Another advantage of procaine penicillin preparations is the paucity of local reactions from its use. Beeswax, which acts as a foreign substance and which may be antigenic, has been eliminated. The authors have not observed any sensitivity to procaine penicillin.

Minimal local reactions and no systemic reactions were observed, even though 29 patients received a second course.

It is concluded that procaine penicillin is a superior preparation for repository penicillin therapy since it does not require the use of dry syringes and needles, is followed by very few local reactions, and results in more prolonged blood penicillin concentrations than any penicillin preparation yet studied. (J. Lab. and Clin. Med., Oct. '48 - J. A. Robinson et al.)

* * * * * *

Preliminary Observations on the Use of Human Arterial Grafts in the Treatment of Certain Cardiovascular Defects: For many years surgeons have felt the need for some technical procedure that would help in bridging gaps of the arterial system when a large vessel has been destroyed by trauma or has become thrombosed because of degenerative disease or embolism, or when certain cardiovascular abnormalities require operative correction.

In experimental studies, aortic segments were taken from donor dogs and stored in flasks, the vessel being just covered with an electrolyte solution, to which had been added glucose (1 percent) and dog serum (10 percent) and a buffer, as well as penicillin and streptomycin (giving a concentration of 50 units of each per cubic centimeter), and finally a phenol-red indicator so that changes in the reaction of the solution could be determined by inspection of the fluid in

the flasks. Each flask with its solution containing a segment of vessel was stored in an icebox, the temperature of which did not range beyond from 1 to 4° C. Tissue-culture studies on segments of vessels preserved in this way showed that vessels were viable for as long as from 35 to 40 days in most cases. Segments of vessel that had been stored in this manner for periods of from 2 to 98 days were implanted into recipient dogs. Twenty-four such grafts were made, and the recipient animals kept from 4 days to 10 months. There were no deaths from dehiscence or thrombosis of any of the grafts. Three animals had minor thrombi at the lines of anastomosis. The grafts were known to be carrying blood for periods as long as ten months. These vessels were studied in the living dogs by aortagrams, and were carefully studied at autopsy after death or sacrifice of the animals. The experiments indicated that arteries can be stored satisfactorily by this method in the cold for slightly more than a month and can still be used for purposes of grafting.

It was believed that this method of arterial preservation might be applicable for vessel grafting in human subjects. Segments of arteries obtained within a few hours from human beings who had died in automobile accidents were collected under aseptic conditions and stored for use whenever the need for such an arterial graft might arise. Nine such grafts were used to bridge gaps between the aortic system and the pulmonary artery when it was desired to establish an aorta-pulmonary artery shunt for alleviation of the cyanotic state of the tetralogy of Fallot, and when it was impossible directly to anastomose vessels of the aortic and the pulmonary systems by the Blalock or the Potts technic. One of these patients died twelve days after operation, largely from the effects of dicumarol therapy. A second died two days after operation from cardiac decompensation. The graft in each case was patent at postmortem examination. In the 7 surviving patients the grafts are apparently carrying blood and have been in place for from one to 5 months. Evidence that these grafts are patent can be adduced from the fact that all the children have continuous murmurs, which previously did not exist, and that the cyanotic states have been markedly improved.

In 3 additional patients, segments of preserved human aorta have been used as grafts during surgical correction of coarctation of the thoracic aorta. Although it is usually possible to excise a narrowed segment of aorta and directly anastomose the remaining ends, removal of the constricted areas from these 3 subjects left very long gaps in the aorta, which precluded reuniting the remaining aortic ends. In each case a graft about 5 cm. in length was employed, and in each case a lumen of full size was established for the aortic pathway. All 3 patients survived operation; they have had relief of the hypertension that existed preoperatively in the upper portions of their bodies, and a greatly increased blood flow to their legs has now developed. These grafts have been in place for only two or three months.

It is too soon to give any final evaluation of the technic of blood-vessel grafting in human cases. However, the early postoperative results are very

encouraging, and they certainly warrant further trial and study when no other means are available for satisfactorily bridging a gap in a large vessel of the arterial system. (New England J. Med., 14 Oct. '48 - R. E. Gross et al.)

* * * * * *

The Healing of Resistant Skin Ulcers After Treatment with Nitrogen Mustard: At the II Medical Clinic of the Jagiellonian University, Cracow, Poland, it was observed in the course of an investigation on the therapeutic value of nitrogen mustard that skin ulcers, resistant to all previous forms of treatment, started to heal. These properties of nitrogen mustard, to the author's knowledge, have not been heretofore described in the literature.

Nitrogen mustard was being used in the treatment for a 23-year-old patient who had a neoplasm of the spine and also a large decubitus ulcer. Although the nitrogen mustard had no therapeutic effect on the neoplasm, the ulcer was covered in from 5 to 10 days with epithelium, and the pain had decreased.

Another case concerned a patient, 42 years old, who had undergone an operation for carcinoma of the penis followed by irradiation with large doses of x-ray in the inguinal region. After the last series of irradiations in February 1947, an ulceration appeared in the right groin and in spite of various forms of treatment, it continued to spread and deepen. He was admitted to the clinic in September 1947 with a widespread and deep lesion affecting three fourths of the right groin. Nitrogen mustard treatment was instituted after determining his sensitivity by the aid of a skin test developed in the laboratory.

After the patient received 6 mg. of the drug intravenously daily for 6 days the pain disappeared, the floor of the ulcer was covered with granulation tissue, and the edges showed a marked tendency to contract. After an interval of six weeks, he received a series of 3 doses of nitrogen mustard (6 mg. daily for 3 days); then six weeks later he received 2 more doses (6 mg. daily for 2 days). The lesion continued to decrease in size, and as the granulation tissue extended to the level of the adjacent skin, it became covered with epithelium. By the middle of November the area of the ulcer was about one half its original size, and 18 weeks after nitrogen mustard therapy, it was about one sixth of its original size.

The author has made similar observations in other cases and found that nitrogen mustard affects superficial decubitus ulcers as well as deep skin ulcerations resulting from x-ray burns.

The skin test for sensitivity to nitrogen mustard is performed as follows. After removing all traces of fat from the skin of the forearm, one drop each of 1-percent, 0.1-percent, and 0.01-percent alcoholic solution of nitrogen mustard is applied to the surface of the skin and the changes are observed after

24 and 48 hours. The skin to which the solution has been applied becomes red in most cases after 24 hours. When the reddening appears in the place where 1-percent solution has been applied, the reaction is regarded as postitive (+); when reddening appears with 0.1-percent solution, it is a strong positive reaction (++); and with 0.01-percent solution, it is a very strong positive reaction (+++). In very strong positive reactions a wheal may appear.

In the author's experience these skin tests have proved of value in determining the dosage of nitrogen mustard. In the majority of cases the authors have observed that the systemic toxic symptoms run parallel to the skin tests. Patients with a +++ reaction tolerated only 0.025 mg. per kg. of nitrogen mustard; those with a ++ reaction tolerated 0.05 mg. per kg., and those with a + reaction tolerated 0.1 mg. per kg.

These observations are submitted as a preliminary report. Further investigations are being carried out on the response of other nonmalignant types of lesions of internal organs to nitrogen mustard. (Am. J. M. Sc., Sept. '48 - J. Aleksandrowicz)

* * * * * *

Use of Silicone-Treated Needles in Blood Donation: In 1946, Jaques and his colleagues reported the use of a silicone (General Electric Dri-Film No. 9987) in the experimental prevention of clotting of blood. In whole blood in contact with silicone-treated surfaces, coagulation was inhibited without the use of anticoagulants for periods of from one and one-half to six hours.

In an attempt to reduce the clotting in the collection of blood for transfusion, needles for intravenous use were treated with silicone and the results compared with untreated needles under controlled conditions. Comparisons were made in two separate clinics held on two different days. One nurse-technician performed all the venipunctures for each clinic.

Equipment used was the standard blood collection sets of the Canadian Red Cross Blood Transfusion Service, which are essentially the same as the equipment of the Medical Research Council of Great Britain as described by Brewer. Blood was collected by gravity flow, no vacuum being used. The intravenous needles were gauge 15 with hollow-ground medium bevels.

G. E. Dri-Film is supplied in liquid form. On exposure to the surface, hydrochloric acid is released and must be washed free. The needles were treated in the following manner: Dri-Film (silicone) was "syringed" through the needles. The excess silicone was removed with a cloth-covered, motor-rotated stylet, and the needle was then syringed with pyrogen-free, sterile, distilled water and repolished. After assembly, the taking sets were autoclaved (25 pounds for thirty minutes). Autoclaving had no visible effect on the efficiency of the silicone coating in the maintenance of a dry surface.

Blood was collected in 94 bottles with the use of untreated needles. Eleven bottles were incompletely filled and 29 contained visible clots. Blood was also collected in 91 bottles with the use of silicone-treated needles. Four bottles were incompletely filled and 10 contained visible clots. There was, therefore, a significant and consistent improvement in yield with the use of silicone-treated needles.

There was also significant increase in the rate of flow. Remarkably consistent net rates per 100 ml. of blood were shown for each clinic with both treated and untreated needles. The rate of flow through the silicone-treated needles was 11.3 seconds per 100 ml. faster than through the untreated needles.

With the use of untreated needles, clotting in the rubber tubing on completion of the donation was frequently so rapid that specimens for Kahn and serologic tests were obtained with difficulty. No clotting occurred when the silicone-treated needles were used, and full specimens were collected easily and rapidly.

Silicone treatment of glass and other surfaces has a number of practical applications in both technical laboratory procedures (in which paraffin or vaseline was formerly used) and in clinical technics, particularly in the prevention of clotting within cannulas and syringes, as in exchange transfusions in the treatment of erythroblastosis fetalis. (Am. J. Clin. Path., Sept. '48 - W. G. Rice)

* * * * * *

The Effect of Intravenously Administered Aminophylline on the Capacity for Effort Without Pain in Patients with Angina of Effort: The literature on the effect of aminophylline on the capacity for effort without pain in patients with angina of effort is conflicting. Although there seems to be little doubt that aminophylline is a coronary vasodilator, there is considerable doubt whether the usual oral doses are absorbed in sufficient concentration to prove of significant value in the treatment of the angina of effort. There seems also to be some doubt concerning the effectiveness of the coronary vasodilatation after intravenous injection. This study concerns the latter problem.

In a series of experiments on patients with unequivocal angina of effort, planned to eliminate conflicting factors in the interpretation of the results, it was found that an intravenous injection of 0.24 Gm. of aminophylline increases the capacity to walk steps without pain. There are fairly marked individual variations in this response. The statistical analyses of the data leave little doubt that the effect of aminophylline obtained is a significant one. There were two sets of data, one in which the sequence of comparisons was saline-aminophylline, and the other in which the sequence was reversed, aminophylline-saline. The highly significant difference between saline and aminophylline which appeared in the first series of experiments was absent when the sequence was reversed, adding further weight to the observation that intravenously administered aminophylline exercises a specific

effect in increasing the capacity for effort without pain, an effect which lasts longer than one hour, for it was still present when the subsequent experiments with saline were performed. In translating the statistical significance of the observations made into practical terms, it is very certain that there is an increase in performance in patients administered aminophylline intravenously over those given saline; it is fairly certain that the increase is about 16 percent; it is not at all certain that the increase is any more than 16 percent.

It should not be inferred, therefore, that the results obtained in these experiments justify the free use of aminophylline by oral administration or even by intravenous injection for the relief of effort angina. Nitroglycerin, taken sublingually, is very effective in obtaining coronary vasodilatation and increased capacity for effort without pain, and a tablet taken under the tongue is more convenient than an intravenous injection. The question concerning which of these measures produces a greater and/or longer lasting effect remains and is the subject of another investigation. (Am. Heart J., Oct. '48 - H. Bakst et al.)

* * * * * *

Men Who Contract Venereal Disease: This pilot study is an analysis of data concerning patients in American Army hospitals in Italy during the war.

The source material for the study - 350 soldiers - includes 200 men with venereal disease and, as a basis for comparison, 100 men in the medical and surgical wards of a general hospital, and 50 men hospitalized because of psychoneuroses. In addition, the case records of up to 4,000 white and Negro patients were studied to obtain information regarding purely objective data.

With the group of 350 soldiers, the questions were directed to the men individually, and exact answers were required. Because of the personal nature of the study, it was felt that personal interviews, carefully conducted, would secure more valid results than would be possible by studying the entire group by more impersonal methods. The men were made aware that they were helping to solve a war problem. They cooperated well.

The following general conclusions were drawn from the data obtained:

1. There seems to be no difference in the type of religious affiliation between white patients with venereal disease and the white control group.

2. Among the white soldiers, there was as large a percentage of noncommissioned officers in the group with venereal disease as in the control group.

3. Soldiers with relatively little education, both white and Negro, were more likely to contract venereal disease than those who had finished high school or gone to college.

4. Among both white and Negro soldiers, the group of patients with venereal disease contained a higher percentage of men with records of repeated arrests in civilian life and with records of punishments while in the army.

5. The patients with venereal disease, in both white and Negro groups, included a higher percentage of single men.

6. In both the white and Negro groups a higher percentage of men with venereal disease than those not having venereal disease visited professional prostitutes while in civilian life, indulged in extramarital sexual intercourse, both as civilians and as soldiers, and began heterosexual intercourse in less than 3 months after overseas duty began. The men with venereal disease had intercourse more often than those of the control group.

7. The patients with venereal disease, in both the white and Negro groups, included a higher percentage of men who were heavy drinkers than were included in the control groups. Of the white patients, 2 percent of the control group and 9 percent of the venereal disease group were heavy drinkers. Of the Negro patients, 6 percent of the control group and 23 percent of the venereal disease group were heavy drinkers. Of the neuropsychiatric group, 4 percent were so classified.

8. No differences in civilian occupation nor in regularity of employment in civilian life were shown between the patients with venereal disease and the control groups in either white or Negro soldiers.

9. There was a difference in the average age at which men in each group first experienced heterosexual intercourse. In both Negro groups, this average was 14 and 1/2 years; in the white venereal disease group, 16 years; in the white control group, 16 and 7/12 years; and in the psychoneurotic group, 17 and 4/12 years.

10. All the men were asked whether they believed sexual intercourse is necessary to maintain good physical health. Many were uncertain. Thirty-six percent of the white venereal disease group replied in the affirmative, as did 12 percent of the white control group and 50 percent of the Negro group. Asked whether they believed masturbation to be injurious to health, 74 percent of both the venereal disease groups replied in the affirmative, as did 55 percent of both control groups.

In addition to the statistical material presented, a number of impressions were gained concerning the behavior patterns of these men with venereal disease.

The patients of the venereal disease groups were less discriminating than those of the control group regarding the females with whom they chose to cohabit. Men with venereal disease more frequently cohabited with a professional prostitute,

but those in the control group more often sought to acquire what they called a "friend" or "acquaintance." The members of the venereal disease groups more frequently decided to have sexual relations on the spur of the moment, after being solicited.

There was no relationship between neurotic personality and the contracting of a venereal disease, except in isolated instances. These isolated cases showed indication of personality problems without sufficient evidence to warrant a diagnosis of psychoneurosis. Some of these men complained of inability to have sexual intercourse while using a condom. Others felt threatened by prolonged abstinence, feared they would lose their potency, and felt compelled to indulge in sexual activity to prove their masculinity. This fear of loss of virility was commonly expressed by nearly all groups of soldiers. One gained the impression, however, that patients with venereal disease felt more insecure than the average person and to them sexual intercourse was a reassurance and proof of their manliness.

A diagnosis of psychopathic personality was made in very few instances, but the number was probably greater than that found in the wards of any general hospital.

There was a positive relationship between venereal disease and one psychiatric entity, namely, intellectual deficiency. A number of men, mentally deficient, not necessarily sexually aggressive, visited prostitutes mainly through the influence of fellow soldiers. This same group did not have the intellectual capacity to apply sensible precautionary measures.

In summary, the following is the picture of the soldier who contracts venereal disease. He has less education than other soldiers. He is more often single, is more unrestrained, carefree, ready to take chances, and more easily influenced. He drinks a little more, and as a civilian was arrested somewhat more frequently. He does not adjust quite as well to army life and receives more courts-martial and company punishments. He begins his sex life somewhat earlier, and as a civilian more often engaged in extramarital intercourse and more often visited professional prostitutes. As a soldier overseas, he began his heterosexual experiences earlier and indulged more frequently. Sexual intercourse is a more important factor in his life and he shows less discrimination regarding the woman with whom he cohabits. He less often selects the woman but is readily solicited by her. (J. VD Information, Nov. '48 - M. W. Brody)

* * * * * *

Therapy in Acute Fluoride Poisoning: Fluorosis may categorically be divided into 3 types:

a. Chronic, low-dose poisoning, giving rise to dental defects and perhaps to other less well understood phenomena. This type of poisoning is not known

to cause physical incapacitation, and is primarily the result of ingestion of excessive amounts of naturally-occurring fluorides in drinking water supplies.

b. Chronic, high-dose poisoning, resulting in bone disease (Roholm's "cryolite fluorosis") and other afflictions which may seriously affect the victim's subjective well-being. This type is usually associated with industrial exposure of workers, or of the inhabitants of industrial regions.

c. Acute fluoride intoxication due to ingestion or inhalation of relatively large amounts of fluorine in elemental form or in chemical compounds.

The third form, acute fluoride intoxication, has not been examined with the same vigor that has characterized the investigation of the other two. It has therefore seemed advisable to employ a case report as the framework for a discussion of certain pertinent aspects of the acute type of fluorine poisoning.

F.B.M., No. A57262, a 16-year-old, white, unmarried, schoolgirl-store-clerk, was brought to the emergency room of the New Haven Hospital on 8 October 1946, at 9:45 a. m. Twenty minutes earlier she had taken poison, which she admitted was one third or one half of a drinking glass of roach powder mixed with water.

The patient was a well-developed and nourished, acutely ill, white, adolescent female, appearing somewhat older than her stated age; T. 99.6, P. 80, R. 16, B.P. 120/80. She lay motionless on a stretcher, responding dully and reluctantly to questions. At intervals she was racked by abdominal cramps which caused her to writhe and cry out in pain; these were usually followed by emission of cloudy opalescent, bright green vomitus and involuntary watery diarrhea. The skin was dirty and pale with marked erythema and slight induration at sites of contact with vomitus on face, neck, and chest. The mucous membranes were quite pale. There was periodic emission of a watery mucinous discharge from the nares mixed with vomitus. Salivation was profuse and watery. The pharynx was injected. Respiratory motions were slow and shallow. The lung fields were clear except for loud, coarse tracheal ronchi. Aside from tachycardia, precordial signs were not revealing. A tense, scaphoid abdomen emitting grossly audible peristaltic rushes at from 1- to 5-minute intervals was tender throughout, even to light touch.

The immediate impression in the emergency room staff was that the poison had been arsenic. The stomach was washed and magnesium sulfate administered by tube. The author saw the patient 30 minutes after admission, and in the interim the pulse had risen to 100, respirations had fallen to 12, and the blood pressure was 100/70. Intravenous injection of 1,000 c.c. of a 5-percent solution of glucose in distilled water was started. Because the blood pressure continued to fall, 500 c.c. of pooled plasma was started at 11:30 a. m. Shortly thereafter it was found that the poison substance had been sodium fluoride roach powder, a legally-required pigment in it accounting for the bright green color of the vomitus.

Lime water (0.15 percent $Ca(OH)_2$) was immediately obtained and 4 ounces administered by mouth, followed by 1 ounce every 30 minutes for the next 12 hours. A continuous intravenous infusion of alternating glucose solution and of normal saline (plus 1 pint of whole blood) was maintained during the first 24 hours to combat enteric fluid loss and shock. This included 2,500 c.c. of 10-percent glucose and 1,000 c.c. of normal saline, making a total parenteral fluid intake of 5,500 c.c. During the first 2 hours of treatment the patient improved noticeably, although the temperature rose to 102 and acute discomfort continued. Digifoline (8 cat units) was administered intravenously to facilitate full digitalization should indications appear, but none developed.

Calcium gluconate was kept in a syringe at the bedside, and when some 4 and 1/2 hours after admission, the patient developed positive Chvostek and Trousseau signs and complained of numbness and tingling of the extremities, two ampules were administered intravenously, with prompt relief. Additional calcium gluconate was administered in the continuous infusion during the first night. Later in the afternoon the patient vomited up bright red specks of tissue, one or two of which measured as much as 1 by 0.5 by 0.25 cm. On microscopic examination these proved to be plates of mucosal epithelium, presumably gastric. Examination of a blood sample for hemolysis at this time was negative. The local erythema of face and chest ("vomitus burns") was still noticeable 7 hours after admission.

The next morning (24 hours after poisoning) the patient was dramatically improved. Although complaints of aching and tingling of the arms suggested recurrence of tetany, absence of other signs caused this to be ascribed to frequent venepunctures and to the intravenous infusions. A subsequent determination of serum calcium confirmed this. A liquid diet was given, and on the 3rd hospital day a full diet was resumed. Temperature returned to normal 48 hours after admission, and on 11 October the patient was sitting up in a chair virtually recovered.

The simplest effect of fluorine on the animal organism is a corrosive one, seen on skin contact, inhalation, or ingestion of volatile or soluble fluorine compounds. This effect consists of superficial or deep erosive burns of skin or of respiratory or digestive-tract mucosa. In the case of F.B.M., this effect was apparent both on the skin areas in contact with vomitus and later from the vomiting of digestive tract epithelium. A specimen of the vomitus, sealed and stored in the refrigerator for medico-legal purposes, was subsequently found to have etched the glass vial in which it was placed. Presumably the reaction with gastric contents proceeds as follows:

$$NaF + HCl \quad HF + NaCl.$$

It is probably justifiable to assume that the intense intestinal activity with cramps, borborygmus, vomiting and diarrhea, all common symptoms of acute

poisoning seen in this patient and repeated in others, are the result of this corrosive effect. It is also likely that the renal irritation and the kidney damage noted at autopsies are attributable to the same mechanism, accentuated by concentration of the fluorine compounds by the excretory mechanism.

A less immediate but equally important effect of large doses of fluoride, once it has entered the circulation, is its combination with calcium to form the insoluble salt $CaF_2$. This effect in the test tube has been utilized for the prevention of clotting of blood. In the intact animal or in humans the effect on clotting apparently is not an important factor in the outcome of acute poisoning, although a relationship between coagulation time and chronic, low-dose fluorosis has been recorded. One group reports that coagulation of the blood is actually increased in fatal human poisoning. This observation may represent increased viscosity secondary to shock rather than a specific fluoride effect. The author and his associates have noted a similar phenomenon in rats. It seems most probable that hemorrhagic phenomena noted by many observers in intestinal mucosa at autopsy are secondary to local corrosive action rather than to any generalized vascular reaction or clotting disturbance. A prothrombin time determination on F.B.M. was normal. No bleeding tendencies were noted. A coagulation time was technically unsatisfactory and is not reported.

The most dangerous clinical result of this biological inactivation of calcium is tetany which may, and frequently has, ended in death, although the tetanic nature of agonal motor disturbances has not always been recognized. It seems probable that many of the "convulsive" phenomena reported in fatal fluorosis were unrecognized tetanic states. The appearance of tetany is usually delayed for from 3 to 6 hours after ingestion. Oral and parenteral calcium are therefore important adjuncts to therapy, the former to intercept unabsorbed fluoride, the latter to replace precipitated serum calcium. The efficacy of such therapy was demonstrated in the case of F.B.M. whose clinical tetany, appearing after a typical time interval, disappeared promptly on administration of calcium gluconate. Unfortunately, it was not possible to obtain a serum calcium level until 24 hours after therapy. Others have demonstrated similar improvement in the treatment of human cases and in animals, (although no effects are demonstrable with small doses). The time interval between fluoride exposure and the onset of tetany is so short that it is improbable that one is dealing with gastric tetany. Nevertheless, chloride loss from emesis undoubtedly contributes in part to the depletion of ionized serum calcium.

Reported cases of fluoride poisoning are predominantly accidental in origin. Crystalline or powdered sodium fluoride, the commonest offender, resembles many common kitchen comestibles, and it has been mistaken for baking soda, Epsom salts, baking powder, powdered milk, Rochelle salts, starch and laxative salts.

The lethal dose of fluoride in humans is not easily determined. As Gettler has pointed out, the dose taken is often unknown and the amount rejected in

vomitus (or diarrhea) may be large. The statement that the aliquot unabsorbed but remaining in the intestines is not contributory to fatality is open to question in view of the intense local irritant action discussed above. Several instances of deaths resulting from the swallowing of from 4 to 5 Gm. of sodium fluoride are available, and from this it is inferred that the average adult, if untreated, will succumb to this dosage. F.B.M. swallowed about 4 ounces of a thicker-than-cream suspension of 95-percent sodium fluoride in water (estimated to have been from 50 to 80 Gm.), the largest dosage from which a human has been known to recover. Undoubtedly much of this was ejected during the early vomiting.

The theoretical considerations noted above offer a basis for logical therapy. The need to identify the nature of an offending poison should always be obvious. In fluoride poisoning this need is accentuated by the high toxicity of fluorides and by the availability of specific therapy.

The physician who identifies the toxic agent as fluoride must still cope with the problem of therapy. The following general outline of treatment is therefore offered as one which seems to be the most rational and life-saving:

1. Act quickly. Fluoride may kill in a few minutes, and from 3 to 4 hours after ingestion is the most frequently reported lethal interval.

2. Start intravenous therapy with glucose in normal saline promptly, both to maintain blood sugar in case of hepatic glycogen depletion, and to have a venous channel available for transfusion. Shock may kill despite calcium.

3. Wash the stomach gently with saline, or preferably with lime water, and then give lime water at frequent intervals.

4. Have calcium available for intravenous administration and watch closely for signs of tetany. Tetanic death is often rapid.

5. Maintain high urine volume with parenteral fluid.

6. Wash away vomitus, feces, and urine promptly to prevent external burns. (Am. J. M. Sc., Sept. '48 - J. H. Peters)

* * * * * *

Spinal Nerve Injury in Dorsolateral Protrusions of Lumbar Disks: The fact that in some cases of sciatica there are no signs of disk herniation at myelography and operative inspection of the spinal canal prompted Lindblom (one of the authors of this report) to make an anatomic study of the incidence of lumbar disk degeneration by postmortem examination. Specimens were taken in 160 cases in which the patient had died at from 14 to 87 years of age, regardless of the history of clinical symptoms and cause of death. Among the specimens, 60 nerve compressions were found, most of them by dorsolateral protrusions against the lateral part of the intervertebral canal, where the nerves

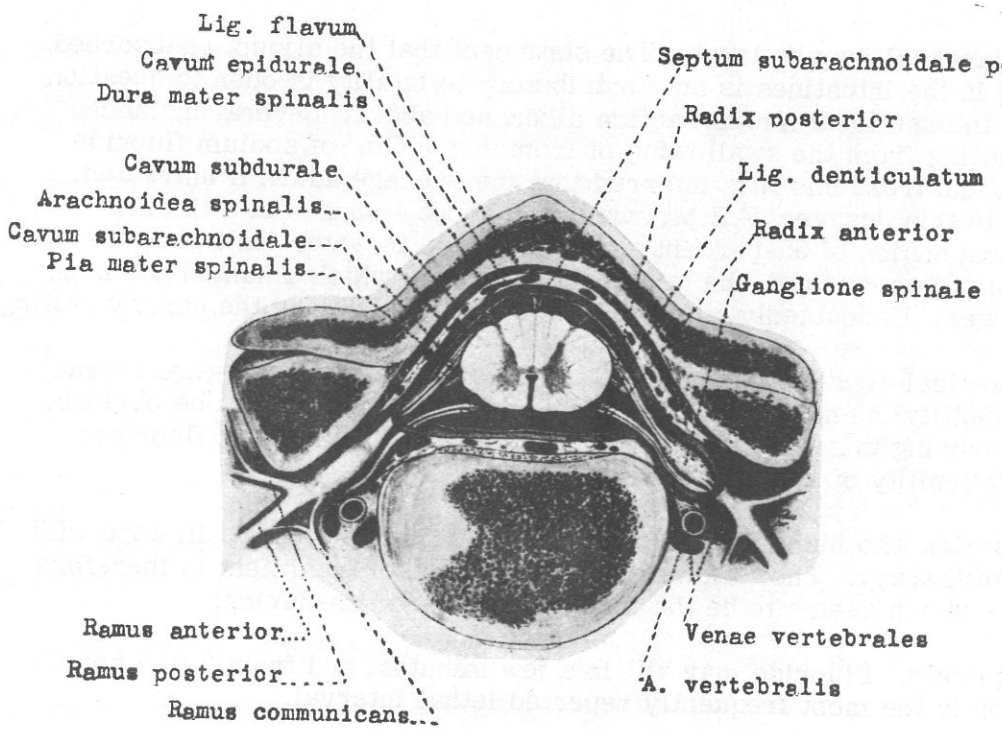


Fig. 1. Schematic cross section illustrating topography of subarachnoidal space, spinal ganglia, roots, and nerves in the intervertebral foramina. From Rauber and Kopsch.

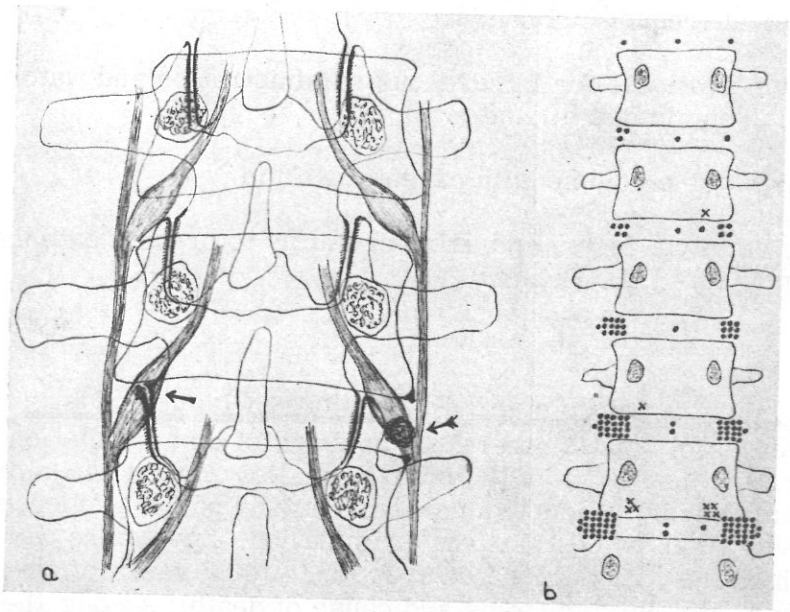


FIG. 2. Frontal view sketches. a, Topography of roots, ganglia, and nerves in relation to lateral disk protrusion (←«), and osteo-arthritic intervertebral joint (←). b, Occurrence of nerve compressions by protruding disks (.) and joints (x) in a material of 160 cases (Lindblom[4]).

with their ganglions cross the corresponding disk (Fig. 2). The incidence of these lateral compressions was found to be correlated to a high occurrence of radial ruptures in dorsolateral direction of the annulus fibrosus of the disks.

The purpose of the present investigation was to determine the extent of nerve damage in the dorsolateral disk protrusion.

In specimens from bodies of young persons without signs of disk degeneration, the spinal ganglion with the adjacent spinal nerve and nerve roots in the region of the intervertebral foramen were surrounded by fat and vessels, and fixed to the surroundings by loose connective tissue only. The cross section of the ganglion and the efferent nerve was quite circular. The disks with definite degeneration had a tendency to protrusion of their margins, especially in dorsal and dorsolateral directions; this agreed with the finding that most of the ruptures occurred in these directions. In cases of ruptured disks that bulged towards the lateral part of the intervertebral foramina, the fat between the disk and nerve tissues was reduced or totally lacking, the ganglions and nerves being more or less flattened or hollowed, in a few cases almost fenestrated by the protruding disk masses. Sometimes the ganglion and the nerve adhered to the protruding disk by dense connective tissue, so that their separation from the disk had to be made with a knife. Red lead injected from the ventral side into the center of the disk passed through the ruptures to the surface of the protrusion and could be found in immediate contact with the nerve tissue. Thus, a communication which might explain the perineural fibrosis between disk ruptures and perineural spaces was demonstrated.

According to the deformity seen macroscopically, the nerve compressions were graded into stages I and II, stage I being a flattening or slight excavation against the disk protrusion, and stage II a definite hollowing or fenestration.

Some cases of protruding intervertebral joints were found in which the protrusion was caused by osteo-arthritic changes. These protrusions were situated far medially, directed towards the posterior side of the nerve roots, and only occasionally caused impressions into the nerve roots.

Material from 17 in the 160 cases was selected for microscopic examination. In all these cases one or more spinal nerves were compressed to varying degrees by dorsolateral disk protrusions. In each case the compressed spinal nerve or nerves and some normal nerves were taken for microscopic study. In order to obtain a control material with similar effect of age, general disease, etc., on the nerves, the normal spinal nerve opposite to the compressed one was always examined, or, if the compression was bilateral, the normal spinal nerves cranial or caudal to the compressed nerves. Often several normal nerves were examined from each case.

The material was obtained within from 24 to 36 hours after death and fixed in 10-percent formalin. The following tissues were chosen for histologic study:

(1) the spinal cord segment of the compressed spinal nerve stained according to Nissl and examined for signs of retrograde degeneration; (2) one or two thoracic cord segments stained according to Kulschitzky in order to bring out ascending degeneration; (3) the proximal parts of ventral and dorsal roots of both normal and compressed spinal nerves stained for axons according to Bodian and for myelin sheaths according to Alzheimer-Mann-Häggqvist (A.M.H.); (4) the spinal nerves sectioned serially from the point of entrance of the roots into the dural sac, through the spinal ganglion and down into the spinal nerve, i.e., well past the compression in the case of compressed nerves. Alternating series were stained according to Bodian (or Davenport) and A.M.H. From the Bodian series sections at regular intervals were stained for connective tissue (Azan or hematoxylin-Weigert-Hansen).

Though the material had been preserved for considerable time (several years in most cases) in the 10-percent formalin solution, the staining qualities were generally satisfactory and in some cases surprisingly good.

The first step in a search for damage to the spinal nerves by dorsolateral protrusions of the lumbar intervertebral disks would be to determine the exact localization of the deleterious pressure. The protrusions in question leave the disk in a dorsolateral direction, and have a chance of reaching the spinal nerve in the depth of the intervertebral canal itself. Here the spinal nerve swerves around the column formed by the vertebral bodies and the intervertebral disks, and its general direction is caudal, lateral, and ventral. In the first part of this stretch, at the entrance into the intervertebral foramen, the dorsal and ventral roots are still separated and are surrounded by a funnel or sac of the dura mater, which slowly closes in on them. More distal the spinal ganglion lies in direct continuity with the dorsal root, and at this level the ventral root is still quite distinct as is easily seen in sections, but difficult to dissect from the spinal ganglion on account of the dense connective tissue surrounding the roots and holding them together. Immediately distal to the spinal ganglion the sensory and motor nerve fiber bundles start to intermingle, thus forming the spinal nerve (Fig. 1). The stretch of nerve, crossing the intervertebral disk in a slanting direction as described above, is at the level of the spinal ganglion and the first part of the spinal nerve. The ventral root lies exactly ventral to the dorsal root at the entrance into the intervertebral foramen. This relative position is retained all the way down to the level where the motor and sensory fibers intermingle. Thus the motor fibers at first lie ventro-medial and more distally they lie medial to the spinal ganglion and the sensory fibers. This means that the motor fibers always lie flanked by the spinal ganglion and the sensory fibers on one side and the intervertebral disk on the other.

When a protrusion of the intervertebral disk bulges dorsolaterally into the intervertebral canal, it will first press upon the ventral root fibers and then on the whole of the spinal ganglion and the spinal nerve, and at the same time it pushes up the entire nervous structure against the dorsolateral margin of the intervertebral canal in the region of the intervertebral joint. Even macroscopically it is easy to see that this pressure deforms the nerves and hollows

them out in the region of the spinal ganglion. The exact point of applied pressure can be determined microscopically. The region where the disk protrusion compresses the nerve always proved to be somewhere on the distal half of the spinal ganglion and the first centimeter of the spinal nerve (Fig. 2,a). The deformation ranged from a slight flattening at a circumscribed area on the nerve to a severe hollowing out of a long stretch of it. In cases with slight pressure the ventral root bundles seemed to be more resistant than the ganglion, but with increasing pressure both ventral root bundles and ganglion became flattened.

When the intervertebral joints were enlarged by osteo-arthritis the nerves were occasionally deformed in two places. The most proximal point of compression was where they were pushed up against the intervertebral joints (Fig. 2,a). This point usually corresponds to the proximal half or the middle of the spinal ganglion, and the deformation is seen in the histological sections as a flattening or even a hollowing out of the ganglion at the side opposite to the ventral root fibers. Further down in the distal half of the spinal ganglion or in the first stretch of the spinal nerve, the direct compression by the disk protrusion is seen (Fig. 2,a). A "secondary" compression from the enlarged intervertebral joint occurred in 8 out of 23 compressed nerves, always together with a "primary" or "direct" compression by the protruding disk. The "secondary" compression was usually slight, though in some cases quite considerable.

The compression was found to have severe effects on the nerves. The type of damage, though varying in severity, is characteristic and the appearance constant in different nerves. The damage is more obvious in the ventral root bundles. The reason is that the motor nerve fibers of the lower lumbar and upper sacral segments, which are those most frequently affected, are mainly large fibers, as shown by Rexed, one of the authors, previously. Degenerative processes are relatively more easily seen where there are fewer small and nonmyelinated fibers.

The basic effect of the compression is degeneration of a greater or lesser number of the nerve fibers. The damage does not occur as a massive, single trauma to the nerves but as many, repeated small traumas. Furthermore, each trauma is not restricted to a sharply localized point but exerts its effect over a relatively large area. As a result, the degenerating nerve fibers are usually seen strewn diffusely all over the cross section in smaller or greater numbers in proportion to the severity and duration of the compression. Also, the state of the degeneration varies from fiber to fiber, some showing signs of a fresh, others of an earlier lesion. Another characteristic feature of these nerve injuries is that as soon as a nerve fiber begins to degenerate there occur reactive regenerative processes. In nerve fibers damaged long ago, regeneration has, of course, progressed far in comparison with that in recently degenerated fibers. The resulting picture is a curious mixture of sound, degenerating, and regenerating fibers. In nerves with little degeneration, these will show up as small patches or islands with proliferated Schwann cells, large and small

regenerated nerve fibers, and varying amounts of degeneration products. In nerves with much degeneration the reacting tissues form more or less continuous fields surrounding the isolated or grouped undamaged nerve fibers. Sometimes the Schwann cells and connective tissue form strange structures reminiscent of the arrangement of cells in certain neurinomas.

The degeneration just described was found at the level of compression and could be followed distally into the spinal nerve. In the most severely injured nerves it was seen to ascend for a short stretch above the actual site of pressure.

The damage to the sensory fibers is, of course, very similar in appearance to that of the motor fibers. However, degeneration is apparently much more infrequent and not as severe. There may be several reasons for this. One is that small myelinated and nonmyelinated fibers are very numerous among the sensory fibers. This makes it more difficult to find signs of degeneration and regeneration in isolated fibers or in very small bundles of fibers. This cannot, however, explain everything. The pressure acts on these nerve fibers in the distal part of the ganglion or in the first stretch of the spinal nerve. Distally, they almost immediately mix with the motor fibers, which, of course, also are damaged in these cases, and it may happen that some degeneration is wrongly ascribed to motor instead of sensory fibers. There is also the possibility that motor nerve fibers on the whole are more damaged than the sensory ones, since the ventral root fibers lie closer to the protrusion (vide supra). As a last factor there is the possibility that the motor nerve fibers generally are more vulnerable than the sensory ones. The amount of degeneration has always been estimated with great caution and it may in reality be greater than has been assumed here.

The spinal ganglion itself and its nerve cells show more obvious reaction to the pressure. The spinal ganglion as a whole is often deformed to a greater or lesser extent. Instead of appearing circular in cross section, it may sometimes appear as a crescent or sickle. This general deformation also influences the cells themselves, which become flattened and deformed, especially near the compressed margin of the ganglion. Some of these cells show definite signs of atrophy and altered staining reactions. In view of the relatively long time between death and fixation of the specimen, however, it was considered useless to examine the cytological details of the ganglion cells, for this might have been misleading. However, not many ganglion cells could have been damaged irreparably, because practically no signs of injury were detected in the proximal parts of the dorsal roots, where a considerable loss of cells would have caused an appreciable degeneration.

The internal organization of the connective tissue of the spinal ganglion was severely deranged. Normally, the connective-tissue septa between groups of nerve cells and fiber bundles are rather insignificant. In the compressed ganglions, however, the amount of connective tissue was much increased and it

formed impressive strands, running as concave septa parallel to the margin of compression. This altered internal organization of the connective tissue seems to be a most sensitive indicator of abnormal pressure on the spinal ganglion.

In the spinal nerve, on the other hand, distal to the ganglion, the reaction of the connective tissue to pressure was much less marked. As stated under the macroscopic findings, the compressed spinal ganglion and nerve were sometimes so strongly adherent to the protruding disk that they had to be separated from it by a knife. Inside the spinal nerve the amount of connective tissue was only slightly increased, even in cases of most severe compression. It was difficult to estimate the degree of reaction here in that the amount of connective tissue inside and around the spinal nerve varied greatly in different normal nerves.

The proximal parts of the spinal nerve roots near the cord were also examined, both with myelin sheath stain and silver impregnations. Significant differences between normal and damaged segments were not found.

Spinal cord segments were examined, with negative results.

In a number of both normal and damaged nerves in these cases a remarkable alteration of the nerve roots at their entry into the intervertebral foramina was noted. This alteration was evidently quite unrelated to the injury caused by the protruding disks and described in this paper. In the small funnel-shaped space, formed when the dura mater closes in on the roots, there could be seen in some cases a pathological thickening and proliferation of the arachnoidea. The circumscribed proliferations resulted, in the most extreme cases, in severe deformation of the nerve roots and were connected with cystic formations in the root fascicles themselves.

The relation between severe macroscopic compression and severe microscopic signs of nerve damage was evident from the results of this study. The nerves that were only slightly compressed macroscopically show either slight nerve injury microscopically or no certain nerve injury at all. The normal control segments show no reaction of the type caused by compression of protruding disks. The only possible exception was a single case in which the spinal roots of the first sacral segment showed bilateral bleeding and degeneration in the absence of a nerve compression. The localization of these processes differs from that of disk protrusions because the nerve injury here occurs in the intraspinal parts of the roots. The type of injury also is different and can scarcely be looked upon as an example of a process simulating nerve damage in the compressed nerves.

Sometimes a "secondary" compression from a pathologically enlarged intervertebral joint adds to the "primary" compression by the protruding disk. In this study this finding was of minor importance, always being the result of the

initial pressure of the protruding disk with only one exception. The compressions by the joints were sometimes noticed at the macroscopical inspection, but sometimes overlooked, indicating that they were usually slight and did not contribute substantially to the nerve damage. In only 2 cases were these compressions considerable, resulting in definite injury to the nerves.

It was also shown that arachnoidal proliferations and cysts occur as often in segments where the spinal nerve is not compressed as in those with compression. Thus the finding in some cases of both spinal nerve compression and arachnoidal proliferations around the roots evidently is incidental.

It seems highly probable that nerve injuries of the type and extent demonstrated in this study must give rise to appreciable clinical symptoms. Something about the mechanism of such cases may be learned from the paper of Granit, Leksell and Skoglund. They showed that an injured part of the nerve functions as a so-called "artificial synapse," that is, impulses in one set of nerve fibers readily set up impulses in other nerve fibers at this point. At the place of compression the sensory nerve fibers would not only be directly irritated and destroyed by the pressure, but also steady volleys of impulses would be induced in the damaged fibers through the functioning of adjacent sensory or motor fibers.

Direct evidence of the clinical importance of dorsolateral disk protrusions cannot be expected from a study such as this one. These cases were taken at random to obtain an idea of the frequency of dorsolateral protrusions in a large number of persons. Then the effects of these protrusions on the nerves were demonstrated. Lumbago and/or sciatica could be found with certainty in only 6 out of the 17 cases discussed in this paper. The available anamnestic data are too few and too vague to allow of definite conclusions. (J. Neurosurg., Sept. '48 - K. Lindblom and B. Rexed, Dept. of Histology, Karolinska Institutet, and Dept. of Diagnostic Roentgenol., Karolinska Sjukhuset, Stockholm, Sweden)

* * * * * *

The Combined Effect of Potassium Iodide and Streptomycin on Established Tuberculosis in Guinea Pigs: It is a well-known clinical observation that iodides cause Mycobacterium tuberculosis previously absent to appear in the sputum of patients with pulmonary tuberculosis. Jobling and Petersen reported in 1941 that iodine will combine with the unsaturated fatty acids obtained from M. tuberculosis and will neutralize its ferment-inhibiting properties. Subsequent to this neutralization, ferment action ensues within areas of caseation with liberation of the bacillus and its appearance in the sputum. They also stated that iodine might serve another purpose by facilitating the solution and absorption of the caseous matter, thus exposing the bacillus, which otherwise might be inaccessible to the influence of an effective therapeutic agent.

Because of this work and the relatively poor results obtained in the treatment of fibrocaseous tuberculosis with streptomycin alone, it seemed desirable

to test the combined effect of potassium iodide and streptomycin against established tuberculosis in guinea pigs. In one experiment, at the end of four weeks of treatment and the seventh week of infection, all animals were sacrificed and autopsied. On gross examination, the controls and guinea pigs that had been given potassium iodide showed heavy tuberculous infection of all the viscera; in a group that had been given streptomycin, five out of 10 pigs showed spread to the organs, whereas in a group of pigs that had been given streptomycin and potassium iodide, the organs were entirely free from infection.

In a subsequent survival experiment, using young pigs ranging from 350 to 450 Gm. in weight, three groups of guinea pigs were used: 15 in a control group, 15 in a group treated with streptomycin alone, and 16 in a group treated with both streptomycin and potassium iodide. Inoculation with M. tuberculosis (H37RV) was carried out in exactly the same manner as in the preceding experiment. Treatment was started at the end of the fourth week of infection, a week later than in the previous experiment. The potassium iodide dosage was the same as that used in the previous experiment. The streptomycin was increased to three times the former dosage. Treatment was carried on for a period of five weeks and then discontinued. At the end of the twelfth week of infection, 13 of the 15 in the control group were dead, 5 of the 15 in the group treated with streptomycin were dead, and only 1 of the 16 in the group treated with streptomycin and potassium iodide had succumbed. At this time two animals in each group were sacrificed and autopsied for the purpose of obtaining microscopic sections from the three groups simultaneously. Results of microscopic studies will be reported in a future communication. Excluding the two pigs sacrificed from each group, the deaths from tuberculosis at the end of the 15th week of infection were: controls, 13 of 13 animals; the streptomycin group, 6 of 13; the streptomycin-KI group, 2 of 14. The respective mortality percentage rates were thus 100 percent, 46.1 percent, and 14.3 percent.

Clinical tests are now in progress. (Science, 5 Nov. '48 - E. Woody, Jr. and R. C. Avery)

* * * * * *

Examination of the Oral Cavity at Autopsy: The pathologist frequently neglects the oral region in taking routine autopsy specimens. This is unfortunate because oral manifestations occur in a large and important list of diseases, in some of which the oral manifestations are the first to appear. Students and research workers interested in the pathological processes occurring in structures of the mouth are handicapped by the scarcity of suitable autopsy material. It should be abundantly available.

An editorial in the American Journal of Clinical Pathology of August 1948 gives an example of a gap in knowledge particularly important to dentistry, and urges routine examination of the oral cavity at autopsy:

". . . In the dental field the most important problems, of course, are dental caries and diseases that alter the integrity of the supporting structure of the teeth. Teeth may be saved from the ravages of caries only to be lost through disintegration of their normal support. Numerous and elaborate theories (with loopholes) have been propounded to explain periodontoclasia, but none can be accepted or completely discarded in view of our present lack of knowledge. At the present time no one can say with certainty whether alveolar bone, connective tissue, or epithelium is first affected. Until this is determined, one must grope in the dark, seeking the basic factors in the pathogenesis of periodontoclasia.

"The mechanical difficulties (of obtaining oral sections routinely) surely are not insurmountable. A simple technic which is not time-consuming could be worked out whereby tissues for study could be obtained without disfigurement of the body. It does seem that much necessary progress could be made if such studies were made routinely.

"Sections from some portion of the dental arch of persons coming to autopsy, as well as sections from other tissues such as the tongue and buccal mucosa, should be taken routinely, for in no other way can proper correlations be made between manifestations of disease of the mouth and of other parts of the body."

Recently approved dental internships in the armed services and civilian hospitals now provide a body of men who will be working closely with oral and general pathologists. It is expected that this extra body of men will create an increased demand for oral sections, and their training and opportunities will make obtaining them possible. (Pathology Dept., Naval Dental School, NNMC, Bethesda, Md.)

* * * * * *

Laboratory Facilities for Analysis of Radioactive Materials Offered by USPHS: A laboratory for analyzing samples of dusts, water, or other materials for the presence of radioactive substances has been established by the Industrial Hygiene Division, USPHS. In addition to the analytical work, facilities are available for calibrating instruments, and for operating a film badge service. These services will be available to other groups in the Public Health Service and to state and local industrial hygiene groups. The film badges will be supplied and processed on return and the results reported to the interested group. If a preliminary survey indicates potential health hazards, film badges will be furnished to exposed workers in order to obtain a complete record of exposure. (Indust. Hyg. News Letter, Oct. '48, through Indust. Hyg. Digest, Oct. '48)

* * * * * *

Intensive Graduate Course in Otorhinolaryngology, Esophagoscopy, and Bronchoscopy: The Georgetown University Medical Center, Washington, D. C., will sponsor an intensive graduate course in otorhinolaryngology, esophagoscopy, and bronchoscopy. The instructor will be Professor Georges Portmann of the University of Bordeaux, France, who is an outstanding teacher. The course will be of two weeks' duration, beginning 18 April 1949, and will consist of lectures, lantern slides, motion pictures, and demonstrations of operations and examinations on patients and cadavers.

The Bureau of Medicine and Surgery has reserved two places in this course and will pay the tuition for the medical officers chosen to attend. Requests are desired from medical officers of the regular Navy. Applicants must have completed at least two years of formal training or the equivalent in clinical work in otolaryngology and its subspecialties. No service agreement is required. Requests must reach BuMed prior to 1 March 1949 for consideration.

Reliefs are not available for officers selected to take this course of instruction. Authorization orders only will be issued by the cognizant naval district commandants, upon request, for medical officers designated to attend the course.

Further information may be obtained from BuMed by interested medical officers. (Professional Div., BuMed)

* * * * * *

Active Strength of the Dental Corps: Computed on the basis of the existing limitation of two dental officers for each 1,000 persons on active duty in the Navy, there should be 1,081 dental officers on active duty. Actually, however, as of 1 November 1948, there were 802 officers on active duty in the Naval Dental Corps. This number includes 610 dental officers of the regular Navy, and 192 dental officers of the Naval Reserve who have volunteered for, and have been assigned to, active duty for periods of one year or longer. These figures reveal a shortage of 471 dental officers in the regular Navy and a deficit of 279 dental officers now on active duty and required to meet the current needs.

* * * * * *

Op24/cj, EN10/A4-2, Serial: 530P24 25 October 1948

From: Secretary of the Navy
To: All Ships and Stations

Subj: Branch Offices of Army-Navy Medical Procurement Office - Establishment of at Chicago and Oakland

1. The following activities are hereby established, each under an officer in charge:

(a) Chicago Branch
Army-Navy Medical Procurement Office
Chicago Quartermaster Depot
1819 Pershing Road
Chicago, Illinois 4179-200

(b) Oakland Branch
Army-Navy Medical Procurement Office
U.S. Naval Medical Supply Depot
Oakland 4, California 4179-600

These activities are under the military command and coordination control of the Commandant of the Naval District in which located, and are under the management control of the Bureau of Medicine and Surgery, exercised through the Medical Officer in Command, Army-Navy Medical Procurement Office, Brooklyn, N. Y.

2. Bureaus and offices concerned take necessary action.

/s/ John Nicholas Brown
Acting

* * * * * *

BUMED CIRCULAR LETTER 48-117 2 November 1948

To: All Ships and Stations

Subj: Medical Records of Civilian Employees; Disposition of

Refs: (a) BuMed C/L No. 47-170 dtd 11 Dec 1947; AS&SL July - Dec 1947, 47-1147, p. 255.
(b) NCPI Instruction 88 dtd 27 Aug 1948.
(c) Par. 12B11.5(c), Manual of the Medical Department.

1. Reference (a) required roentgenographic chest examinations of all Navy and Marine Corps civilian employees. Reference (b) provides general regulations for the medical care of these employees by the Navy.

2. Effective servicing of inactive medical records of civilian employees of the Navy requires that such records be physically located close to the inactive civilian personnel records. Accordingly, the Industrial Health Jackets (including all records of medical or dental examinations, as well as 14 x 17 X-ray films) of civilian employees of the Navy and Marine Corps, shall be transferred to the Naval Records Management Center, Mechanicsburg, Pennsylvania, one year after the employee's separation or transfer outside the Navy. Requests for information from these records will be processed at the Center in accord with reference (b).

3. An item to cover the disposition of Industrial Health Jackets will be added to reference (c) in the near future.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-118 Joint Letter 5 November 1948

To: All Ships and Stations

Subj: Aviation Selection Tests; Modification of Requirements

Ref: (a) BuPers-BuMed Joint Ltr BuMed-537-HJO-as BuPers A21/P11-1 dtd 14 May 1948.

1. Reference (a) is hereby cancelled.

2. Effective this date all applicants for flight training, officer, enlisted and civilian, will be required to obtain the following scores on the flight aptitude rating tests: ACT, C; MCT, C; FAR, D.

3. All previous instructions in conflict with these requirements are hereby modified.

--BuPers. T. L. Sprague --BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-119 5 November 1948

To: All Naval Hospitals, Hospital Ships, and Hospital Corps Schools

Subj: Utilization of Medical Training Films and Film Strips: Report of

Ref: (a) NavMed P-150, Catalog of Medical Training Films, (Revised April 1948).

1. The Bureau of Medicine and Surgery recently conducted a survey on the availability and utilization of medical training films and film strips. As a result of this survey, it was determined that the utilization of medical training films and film strips is below the standard deemed necessary for adequate training of all medical department personnel.

2. Reference (a) lists 116 Navy produced medical training films and film strips. It is desired that these training aids be utilized to the fullest extent to further the training of medical department personnel. All Navy medical training aids are available on a loan basis from the local Training Aids Library. Permanent copies of films will be granted in cases where the loan distribution, as provided by the Training Aids Libraries, fails to meet the demands of the requesting activities.

3. In order that the Bureau of Medicine and Surgery may be cognizant of the over-all utilization of medical training films and film strips, each addressee is directed to report by letter, the information requested below, on 30 June of each year.

MEDICAL TRAINING FILMS AND FILM STRIPS ON HAND

| Identification No. and Title of Medical Training Aid | No. of Prints on Hand | No. of Screenings | No. of Personnel Viewing Film |
|---|---|---|---|

MEDICAL TRAINING FILMS AND FILM STRIPS PROCURED FROM TRAINING AIDS LIBRARY ON A LOAN BASIS

| Identification No. and Title of Medical Training Aid | No. of Screenings | No. of Personnel Viewing Film |
|---|---|---|

4. Comments and recommendations relative to the distribution, availability and utilization of medical training films and film strips are desired.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-120 8 November 1948

To: All Ships and Stations

Subj: Venereal Disease Educational Leaflets: Availability of

Refs: (a) G. O. #225
(b) BuPers C/L 76-48; N.D. Bul of 30 Apr 1948, 48-308.

1. The series of venereal disease educational leaflets which have been distributed to the Service should be utilized for general education of all naval and Marine Corps personnel in the cause, effect, and prevention of venereal disease. Display and distribution may be made through wall racks, while men are assembling for venereal disease educational movies, after lectures, or they may be used as the basis of a short lecture and discussion by non-medical personnel with small groups of men.

2. The following leaflets are now available and will be stocked at all District Publications and Printing Offices for distribution as requested on the basis of one per five men:

NavMed-1240 (Nov-47) CHANCROID
NavMed-1241 (Nov-47) SYPHILIS
NavMed-1242 (Nov-47) GONORRHEA
NavMed-1280 ( Jun-48) GRANULOMA INGUINALE
NavMed-1281 ( Jun-48) LYMPHOGRANULOMA VENEREUM

3. Additional educational material is being prepared for use in the venereal disease educational program which will assist those responsible for administering the program.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-121 8 November 1948

To: All Medical Department Activities

Subj: Shipment of Personal Effects of Deceased Active Duty Naval Personnel

Refs: (a) Advance notice of change to the Navy Shipping Guide, Change No. 82.
(b) Article 908(4), N. R.
(c) Paragraph 3428.1, Manual Medical Department.

1. Effective immediately transportation of personal effects of deceased active duty naval personnel shall be made in accordance with instructions in reference (a), which is quoted below for the information of all concerned:

art. 1820-6(b) Revised

(b) Effects of deceased personnel. - Transportation of effects of deceased officers and enlisted personnel of the Navy and of officers and enlisted personnel of the Naval Reserve who die while on

duty is authorized. When the remains are shipped by express and when personal effects accompany the remains, the Railway Express Agency allows up to 150 pounds as free transportation; the cost of shipment of personal effects accompanying the remains which weigh in excess of 150 pounds must be borne by the next of kin. Therefore, in packing effects the weight will be kept within 150 pounds, if possible. When there is no doubt as to the next of kin of the deceased, personal effects within the continental United States will be shipped as soon as possible without awaiting specific authorization from the Navy Department. Personal effects returned from points outside continental United States in the Atlantic Ocean area will be forwarded to the Supply Officer, Naval Supply Center, Norfolk, Virginia, and in the Pacific Ocean area to the Personal Effects Distribution Center, Naval Supply Depot, Clearfield, Ogden, Utah.

2. Appropriate changes are being made in the Manual of the Medical Department (ref. c) and it is expected that they will be ready for release to the naval service in the near future.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-122 9 November 1948

To: Commandants, Naval Districts and River Commands

Subj: Venereal Disease Contact Investigation; Request for Training of Interviewers

Refs: (a) BuMed C/L 47-88 dtd 30 Jun 1947
(b) Par. 1521, M.M.D.
(c) Par. 5135, M.M.D.

Encls: 1. (HW) "Interviewer's Aid," NavMed-P-1288
2. (HW) Leaflet, "Why Am I Being Interviewed," NavMed-1282

In this letter the addressees are requested to require each activity of the Navy and Marine Corps to train one or more Hospital Corpsmen, as necessary, for venereal disease contact investigations. Information is given concerning the selection and training of these contact interviewers. The use of the enclosures is explained. The importance of contact investigations together with the prompt submission of the Contact Report (NavMed 171) is stressed.

* * * * * *